

## BIOGRAPHICAL SKETCH

NAME Yidong Bai, Ph.D.	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME baiyidong			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Fudan University, Shanghai, China	B.A.	1985	Microbiology
Shanghai Institute of Cell Biology, CAS	Master Program	1985-88	Genetic Engineering
Columbia University, New York, NY	Ph.D.	1996	Biological Sciences
Caltech, Pasadena, CA	Postdoc	2001	Biology

### A. Personal Statement

Over past 13 years at UTHSCSA, I have trained 7 postdoctoral scholars, 4 PhD students and 5 master students. I have published more than 50 papers together with these fellows in various journals. Among these trainees, five are now faculty members in US, India, Nigeria and China; two are senior research scientist in other US institute (Harvard Medical School and University of Michigan); one is now a postdoc fellow at Stanford University. I also have experiences in training summer undergraduate research fellows and high school students including several minority students. One of the minority student supported by a NIH diversity supplementary grant successfully defended her master thesis, and is now a PhD student at NIH/Brown graduate program in Neurosciences. In particular we have trained many international postdoctoral fellows who obtained PhD/MD from top University in Asia including Xi'an Jiaotong University, Fudan University, Pusan University and Sichuan University. I also have served as co-mentor for PhD students from China, Nigeria and Brazil who came to my lab to do their thesis projects.

### Representative publication published together with my trainees:

1. Song, X., Deng, J.H., Liu, C.J., and **Bai, Y.** Specific point mutations may not accumulate with aging in the mouse mitochondrial DNA control region. *Gene* 350, 193-199, 2005. <http://www.ncbi.nlm.nih.gov/pubmed/15829427>
2. Li, Y., Park, J.S., Deng, J.H., and **Bai, Y.** Cytochrome c oxidase subunit IV is essential for assembly and respiratory function of the enzyme complex. *J Bioenerg Biomembr* 38, 283-291, 2006. <http://www.ncbi.nlm.nih.gov/pubmed/17091399>
3. Deng, J.H., Li, Y., Park, J.S., Wu, J., Hu, P., Lechleiter, J., and **Bai, Y.** Nuclear suppression of mitochondrial defects in cells without the ND6 subunit. *Mol Cell Biol* 26, 1077-1086, 2006. <http://www.ncbi.nlm.nih.gov/pubmed/16428459>
4. Li, Y., D'Aurelio, M., Deng, J.H., Park, J.S., Manfredi, G., Hu, P., Lu, J., and **Bai, Y.** An assembled complex IV maintains the stability and activity of complex I in mammalian mitochondria. *J Biol Chem* 282, 17557-17562, 2007. <http://www.ncbi.nlm.nih.gov/pubmed/17452320>
5. Park, J.S., Li, Y.F., and **Bai, Y.** Yeast NDI1 improves oxidative phosphorylation capacity and increases protection against oxidative stress and cell death in cells carrying a Leber's hereditary optic neuropathy mutation. *Biochim Biophys Acta Mol Basis Dis* 1772, 533-542, 2007. <http://www.ncbi.nlm.nih.gov/pubmed/17320357>

6. Clay Montier, L.L., Deng, J.J., and **Bai, Y.** Number matters: control of mammalian mitochondrial DNA copy number. *J Genet Genomics* 36, 125-131, 2009. <http://www.ncbi.nlm.nih.gov/pubmed/19302968>
7. Park, J.S., Sharma, L.K., Li, H., Xiang, R., Holstein, D., Wu, J., Lechleiter, J., Naylor, S.L., Deng, J.J., Lu, J. and **Bai, Y.** A heteroplasmic, not homoplasmic, mitochondrial DNA mutation promotes tumorigenesis via alteration in reactive oxygen species generation and apoptosis. *Hum Mol Genet* 18, 1578-1589, 2009. <http://www.ncbi.nlm.nih.gov/pubmed/19208652>
8. Sharma, L.K., Lu, J., and **Bai, Y.** Mitochondrial respiratory complex I: structure, function and implication in human diseases. *Curr Med Chem* 16, 1266-1277, 2009. <http://www.ncbi.nlm.nih.gov/pubmed/19355884>
9. Li, Y., Li, H., Hu, P., Deng, J.H., Banoei, M.M., Sharma, L.K., and **Bai, Y.** Generation and Bioenergetic Analysis of Cybrids Containing Mitochondrial DNA from Mouse Skeletal Muscle during Aging. *Nucleic Acids Res* , 38, 1913-1921, 2010. <http://www.ncbi.nlm.nih.gov/pubmed/20022917>
10. Sharma; L., Fang; H., Liu; J., Vartak; R., Deng; J., and **Bai, Y.** Mitochondrial respiratory complex I dysfunction promotes tumorigenesis through ROS alteration and AKT activation. *Human Molecular Genetics* 20, 4605-16, 2011. <http://www.ncbi.nlm.nih.gov/pubmed/21890492>
11. Li, H., Sharma; L., Li, Y., Hu, P., Idowu, A., Liu, D., Lu, J., and **Bai, Y.** Comparative bioenergetic study of neuronal and muscle mitochondria during aging. *Free Radical Biology & Medicine*. 63, 30-40, 2013. <http://www.ncbi.nlm.nih.gov/pubmed/23643721>
12. Vartak, R., Porras, C., and **Bai, Y.** Respiratory Supercomplexes: Structure, Function and Assembly. *Protein & Cell*. 4, 582-590, 2013. <http://www.ncbi.nlm.nih.gov/pubmed/23828195>
13. Vartak, P., Semwal M., and **Bai, Y.** An update on complex I assembly: the assembly of players. *Journal of Bioenergetics and Biomembranes*. 46, 323-328, 2014
14. Porras, C., and Bai, Y. Respiratory supercomplexes: plasticity and implications. *Frontiers in Biosciences*. 20, 621–634, 2015
15. Vartak, R., Deng, J., Fang, H., and **Bai, Y.** Redefining the roles of mitochondrial DNA-encoded subunits in respiratory Complex I assembly. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*. 1852, 1531-1539, 2015
16. Nie, H., He, J., Zhang, F., Li, M., Wang, Q., Lu, J., and **Bai, Y.** Mitochondrial common deletion is elevated in blood of breast cancer patients under oxidative stress. *Mitochondrion*. 1567-7249, 2015. <http://www.ncbi.nlm.nih.gov/pubmed/26678158>
17. Mishur, RJ, Khan, M., Munkácsy, E., Sharma, L., Bokov, A., Beam, H., Radetskaya, O., Borrer, M., Lane, R., **Bai, Y.**, and Rea, S. Mitochondrial Metabolites Extend Lifespan. *Aging Cell* 12439, 2016 <http://www.ncbi.nlm.nih.gov/pubmed/26729005>
18. Jiang, PP, Liang, M., Zhang, C., Zhao, X., He, Q., Cui, C., Liu, X., Sun, YH, Fu, Q., Ji, Y., **Bai, Y.**, Huang, T., and Guan, MX. Biochemical evidence for a mitochondrial genetic modifier in the phenotypic manifestation of Leber's hereditary optic neuropathy-associated mitochondrial DNA mutation. *Human Molecular Genetics*, 2017. <http://www.ncbi.nlm.nih.gov/pubmed/27427386>

19. Etzler, J, Bollo, M, **Bai, Y**, et al. (2017). "Cyclophilin D over-expression increases mitochondrial complex III activity and accelerates supercomplex formation." [Arch Biochem Biophys](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cyclophilin+D+over-expression+increases+mitochondrial+complex+III+activity+and+accelerates+supercomplex+formation) 613:61-68.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Cyclophilin+D+over-expression+increases+mitochondrial+complex+III+activity+and+accelerates+supercomplex+formation>

20. Chen, H., Bai, J., Dong, F., Fang, H., Zhang, Y., Meng, W., Liu, B., Luo, Y., Liu, M., **Bai, Y.**, Abdul-Ghani, MA, Li, R., Wu, J., Zeng, R., Zhou, Z., Dong, LQ, and Liu, F. (2017). Hepatic DsbA-L Protects Mice from Diet-induced Hepatosteatosis and Insulin Resistance. FASEB Journal. In press.

## **B. Positions and Honors**

### **Positions and Employment**

2001- Assistant, Associate Professor, University of Texas, Health Science Center at San Antonio.

2004 - Member, Barshop Institute for Longevity and Aging Research, UTHSCSA.

2010 - Associate Member, Cancer Therapy and Research Center, UTHSCSA.

2014 - Chair, MS Committee of Graduate Studies, Dept. of Cellular and Structural Biology

### **Other Experience and Professional Memberships**

2006 - Editorial Board Member: Frontiers in Biosciences

2011 - Editorial Board Member: PlosOne

2011 - Associate Editor: Frontiers in Genetics

2011 - Editorial Board Member: TheWorldScientificReport

2012 - Editorial Board Member: Mitochondrion

2014 - Editorial Board Member: BBA Molecular Basis of Disease

2015- Regular member, NIH Study Section Neural Oxidative Metabolism, and Cell Death (NOMD)

2012-14 Ad-hoc member, NIH Study Section Neural Oxidative Metabolism, and Cell Death (NOMD)

2015 Ad-hoc Member, NIH Study Section Biology of the Visual System (BVS)

2017 Ad-hoc Member, NIH Study Section Genetics of Health & Disease Study Section (GHD).

2016 Member, NEI Translational Research R24 review Panel

2016 Member, NCI PQ5 R01/R21 Review: mitochondrial heterogeneity

2014 Co-organizer, The pre-meeting of 43rd American Aging Association Conference on "What the role Mitochondria play in Aging".

2014 Faculty member, European Union ITN Marie Curie Project Mitochondrial European Educational Training (MEET) course

### **Honors**

2002 Howard Hughes Medical Institute New Faculty Startup Fund at UTHSCSA

2002 – 04 United Mitochondrial Disease Foundation New Investigator Award

2002 – 07 Ellison Medical Foundation New Scholar in Aging

2004 – 07 American Heart Association Scientist Development Grant

2012, 05 Distinguished Scientists Seminar Program, University of South Alabama 2014, 06

Excellent Review Award (2008-2012), Journal of Genetics and Genomics

## **C. Complete List of Published Work at NCBI and Google Scholar:**

[http://www.ncbi.nlm.nih.gov/sites/myncbi/1DWZ66Uga-nAE/bibliography/47829349/public/?](http://www.ncbi.nlm.nih.gov/sites/myncbi/1DWZ66Uga-nAE/bibliography/47829349/public/?sort=date&direction=descending)

[sort=date&direction=descending](http://www.ncbi.nlm.nih.gov/sites/myncbi/1DWZ66Uga-nAE/bibliography/47829349/public/?sort=date&direction=descending)

<http://scholar.google.com/citations?user=ny0wtXIAAAAJ&hl=en&oi=ao&cstart=60&pagesize=20>

## **D. Research Support**

### **Ongoing Research Support**

1 R01 GM109434-01A1 Bai (PI) 8/1/2014 - 5/31/2018 4.8 calendar

NIH/NIGMS \$1,136,200.00

“Regulation of Mitochondrial Respiratory Complex I Dynamics”

The overall goal of this study is to investigate the regulation of assembly of respiratory complex I.

Role: PI

3 R01 GM109434-01S1 (Bai) 11/1/2014 - 5/31/2016

NIH/NIGMS \$ 75,420.00 Diversity

supplementary.

The overall goal of this application is to support Christina Porras to study the implication of respiratory supercomplex. Role: PI

3R01GM109434-02S1 (Bai) 6/1/2015-5/31/2016

NIH/NIGMS equipment grant [PA15-089], \$181,000

To purchase Metabolic Analyzer Seahorse Role: PI

R01DK076902 (PI, Feng Liu) 4/01/2014- 3/31/2018

NIH/NIDDK

Regulation and Function of Adiponectin Oligomerization Role: Co-Investigator (5% effort)

Barshop Seed Funding Program (PI: Rea Nelson and Bai) 10/15/2015- 8/31/2016

Barshop Institute \$35,000

Genetic and Pharmacological Enhancements of Holo-Complex 1 Assembly Role: Co-PI (1%)

William and Ella Owens Medical Research Foundation grant (Bai) 1/1/2016- 6/30/2017

Owens Medical Research Foundation \$100,000

The regulation of mitochondrial DNA heteroplasmy in tumorigenesis

Role: PI

HSC-CBN PILOT PROJECTS (PI) 1/1/2017-12/31/2017

HSC-CBN \$50,000

GENERATION AND CHARACTERIZATION OF A RETINAL GANGLION CELL MODEL FOR LEBER'S HEREDITARY OPTIC NEUROPATHY

Role: PI

### **Pending Research Support**

1I01BX003502- 01 (Bai) 10/01/2017- 09/30/2021

VA Merit Grant \$600,000

“The implication of mitochondrial DNA heteroplasmy and their shift in tumorigenesis” The overall goal is to investigate the impact of mitochondrial DNA heteroplasmy on tumorigenesis. Role: PI

W911NF- 12-R-0012- 02 (Bai) 05/01/2017- 4/30/2020

Department of Defense \$360,000

“Respiratory supercomplex assembly”

The overall goal of this study is to investigate the assembly of respiratory supercomplex.

Role: PI

1 R01 R01CA219875 Bai (PI) 9/1/2017 - 8/31/2022 NIH/NCI  
\$1,136,200.00

The mitochondrial DNA heterogeneity and tumorigenesis”

The overall goal is to investigate the impact of mitochondrial DNA mutations/variations in colorectal cancer.

Role: PI

**Completed Research Support**

1R21NS072777 08/16/ 20 10-07/31/ 20 14 NIH/NINDS

“Regulation of mitochondrial respiratory complex I”

The overall goal of this study is to isolate nuclear encoded proteins whose over- expression could compensate the mitochondrial dysfunction in cell carrying mitochondrial DNA encoded complex I subunit gene mutations. Role: PI (1%)

1R01AG025223- 01A1 03/01/ 20 06-01/31/ 20 13

NIH/NIA

“Role of Mitochondrial DNA Mutations in Aging in Neuronal Cells”

The overall goal of this study is to study the role of mitochondrial dysfunction and mtDNA mutations during aging mouse neuronal cells. Role: PI

1R03AG024640- 01A2 09/01/ 20 06-08/31/ 20 09

NIH/NIA

“Mitochondrial DNA Mutations in Skeletal Muscles in Aging”

The overall goal of this study is to study mitochondrial dysfunction and mutations in aged mouse muscles. Role: P

During the past 20 years, my research has focused on mitochondria, including the many defects that can arise in the mitochondrial system and how they can contribute to a number of diseases including neurodegenerative diseases. In particular, I am interested in providing a comprehensive understanding of mitochondrial function at the molecular, cellular, tissue and animal levels. Mitochondria play a central role in cellular energy metabolism through the generation of ATP from oxidative phosphorylation. Mitochondria contain their own genomes and have a distinct molecular mechanism governing their gene expression and function. Recent developments have also shown that normally-functioning mitochondria are important in the regulation of apoptosis, signal transduction and cell growth. Mitochondrial defects have been reported in a wide range of conditions, in particularly neurodegenerative diseases including Parkinson's Diseases and Alzheimer's disease. The central theme in the laboratory is to investigate the regulatory mechanisms in mitochondria and the role of mitochondria in regulating various cellular pathways. We have been trying to revisit some basic questions in mitochondrial biology with newly available technology and unique systems established in our own lab, including the dynamics of oxidative phosphorylation machinery (assembly and turnover of respiratory supercomplex), mitochondrial quality control, and maintenance of mitochondrial genome. We have also been trying to establish various cell models carrying different types of deficiencies with different methods including generating cell lines derived from patients with mitochondrial diseases, establishing cell lines carrying mtDNA from old animals with neurodegenerations, targeted disruption of specific mitochondrial protein expression, using chemical to inhibit mitochondrial function, and screening for mtDNA mutations in vitro. With these cell models, we are trying to develop different approaches to remedy the defects including isolation of revertants, genetic repair, pharmacological manipulation and genetic screening by functional complementation.

Emerging evidence supports the proposition that the mitochondrial respiratory chain (MRC) functions via organized multicomplex structures called supercomplexes. However the dynamics and regulation of supercomplex assembly have not been fully investigated. In particular, hardly any regulatory protein factors involved in supercomplex assembly have been identified. The objective of a pending VA grant is to determine if the mitochondrial chaperon, 75 kDa glucose regulated protein (Grp75) plays a role in regulating supercomplex assembly and further to identify additional protein factors involved in this important process.

The dysfunction of mitochondria has long been suspected to play a role in tumorigenesis, and mitochondrial DNA mutations have been reported in various cancers. However, the role of mtDNA mutations in tumorigenesis is still controversial, largely due to the fact that there is no sophisticated system to investigate this subject. With a newly developed system in the lab, we found a mutation in mitochondrial ND5 gene which encodes an essential component respiratory chain, which was also reported in colorectal cancer patients, did play a role in tumorigenesis. In particular, an antagonistic pleiotropy has been associated with this mitochondrial dysfunction associated this mtDNA mutation, and only heteroplasmic mutation (when the mtDNAs are a mixture of both wildtype and mutant) but not homoplasmic mutation (when mtDNA are all mutant) promotes tumorigenesis. On the other hand, disruptive mutations in mtDNA encoding Complex I subunit genes do accumulate in some tumor and cancer cells, in particular in oncocyctic tumors where the unique histological feature is an aberrant accumulation of deranged mitochondria and whose only univocal genetic features are disruptive mutations within mitochondria-encoded genes, particularly those encoding Complex I subunits, which would drive oncocyctic change. We propose to further investigate these seemingly conflicting observations and provide insights to the role of mitochondrial dysfunction and mitochondrial DNA mutations in tumorigenesis.